Summary of Clinical Trial Results

How does a new medicine (efmarodocokin alfa) compare to available medicine and placebo – in people with ulcerative colitis

See the end of the summary for the full title of the study.

About this summary

This is a summary of the results of a clinical trial (called a "study" in this document).

This summary is written for:

- Members of the public
- People who took part in the study

This summary is based on information known at the time of writing.

The study started in October 2018 and stopped early – in December 2021 – because the medicine being studied did not work as well as expected.

No single study can tell us everything about the risks and benefits of a medicine. It takes many people in several studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

- **This means that you should not make decisions based on this one summary**
- **Always speak to your doctor before making any decisions about your treatment**

Contents of the summary

Thank you to the people who took part in this study

The people who took part have helped researchers answer important questions about ulcerative colitis (UC) and the study medicine, "efmarodocokin alfa".

Key information about this study

- This study was done to find out if a new medicine, efmarodocokin alfa, was useful for treating patients with ulcerative colitis (UC).
- In this study, people who had UC were given one of three treatments: 1) the new medicine, 2) an approved medicine, or 3) a placebo that did not contain any medicine.
- It was decided by chance which treatment each person was given.
- This study included 195 people in 16 countries.
- The main finding was that efmarodocokin alfa was not better than the approved medicine. It was not better than the placebo either.
- Thirty out of 172 people taking efmarodocokin alfa had a side effect that doctors thought was caused by the medicine. One person got a serious side effect that doctors thought was caused by the medicine.
- This study stopped early because the medicine being studied did not work as well as expected.

1. General information about this study

Why was this study done?

Ulcerative colitis (**UC**) is a disease of the gut (**colon**). It lasts for a long time (**chronic**) and patients go through cycles of getting better and getting worse. The disease can affect any age group, but peaks between the ages of 15 and 35 years.

UC can cause sores (**ulcers**) in the colon, bleeding through the anus, diarrhea, and stomachaches. It can also lead to even more serious complications (severe bloody diarrhea or toxic megacolon) – that require major, urgent surgery.

There are several medicines used for managing UC:

- Anti-inflammatory medicines
- Immunosuppressants
- Tumor necrosis factor (TNF) inhibitors
- Integrin receptor antagonists

There are other categories of medicines not listed above, some of which have been approved for use in people recently.

The available medicines target the immune system to reduce inflammation in the colon. There are several side effects, and the available medicines are not extremely effective.

Researchers are working to find safer and more effective medicines that do not suppress the immune system in people. They also want medicines that will heal the lining of the colon (**mucosal healing**).

This study was done to find out if a new medicine called, “efmarodocokin alfa”, was useful for UC. Doctors gave efmarodocokin alfa to people with UC, and measured the effect of the medicine on the disease.

What were the medicines being studied?

This study looked at two medicines and a placebo.

Efmarodocokin alfa

- The "**study medicine**" was previously called, "UTTR1147A". It is now called "efmarodocokin alfa".
- It has been given to people in other studies and found to be safe for humans.
- Made by connecting (fusing) two different proteins.
- This medicine could help with mucosal healing in the colon – in people with UC.
- It does not suppress the immune system. Therefore, side effects may be different in comparison to other medicines for UC.

Vedolizumab

- An "**approved medicine**" to which the study medicine could be compared.
- Belongs to a class of medicines known as "integrin receptor antagonists".
- Consists of an antibody directed against a protein (α4β7 heterodimer).
- Works by blocking the action of certain immune cells in the body that cause inflammation ("modulation of innate immunity").
- Approved as a treatment for UC in several countries.

Placebo

- In this study, some people got efmarodocokin alfa or vedolizumab, while others got a placebo.
- The placebo looked like a real medicine but did not contain any real medicine.
- Having the placebo allowed researchers to find out if the treatment given to patients was due to the real medicine.

What did researchers want to find out?

Researchers did this study to compare 3 different treatments given to people:

- The study medicine
- The approved medicine
- The placebo

They wanted to find out how well the study medicine worked in comparison to the approved medicine and the placebo.

They also wanted to find out how safe was the medicine – by checking how many people had side effects and seeing how serious they were.

The main question that researchers wanted to answer was:

1. How well does efmarodocokin alfa work in comparison to vedolizumab and placebo – when given to people with UC?

What kind of study was this?

There are several ways to describe this study.

- **Phase 2 study**
  Phase 2 studies are done to find out if the study medicine is effective for people – who have the disease that the medicine is targeting.
  It also means that the study medicine has already been tested – in an earlier phase 1 study – and found to be safe for use in people.
- **Randomized study**
  A computer randomly decided who joined which treatment group. Researchers and people who took part in the study had no control over this.
- **Double-blind study**
  The researchers and people in the study did not know who was getting which treatment. That made this a double-blind study.
- **Placebo-controlled study**
  Some people got treatments with a placebo. This allowed researchers to compare how people reacted to treatments with the real medicine and with no medicine. That made it a "placebo-controlled study".
- **Parallel-group study**
  This was a parallel group study to compare three different treatments. People were cared for in the same way except that they got the study medicine, the approved medicine, or the placebo. After the study was completed, results for the parallel-group study could be compared with each other to understand the effect of the study medicine, the approved medicine, and the placebo.

When and where did the study take place?

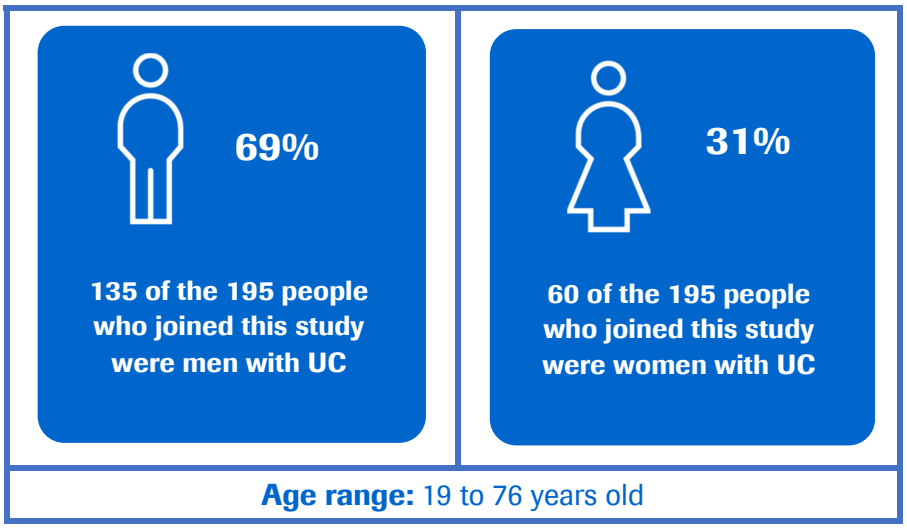
The study started in October 2018 and stopped early because the study medicine did not work as well as expected. This summary presents the results of the study up until it was stopped in December 2021.

The study took place at 71 study centers in 16 countries:

1. Poland (18 study centers)
2. Ukraine (17 study centers)
3. Serbia (7 study centers)
4. Germany (5 study centers)
5. Italy (5 study centers)
6. Russia (5 study centers)
7. Bulgaria (2 study centers)
8. Greece (2 study centers)
9. Spain (2 study centers)
10. United States (2 study centers)
11. Georgia (1 study center)
12. Hungary (1 study center)
13. Ireland (1 study center)
14. Israel (1 study center)
15. Moldova (1 study center)
16. United Kingdom (1 study center)

2. Who took part in this study?

One hundred and ninety-five people with UC took part in this study.



People could take part in the study if they met all of the following conditions:

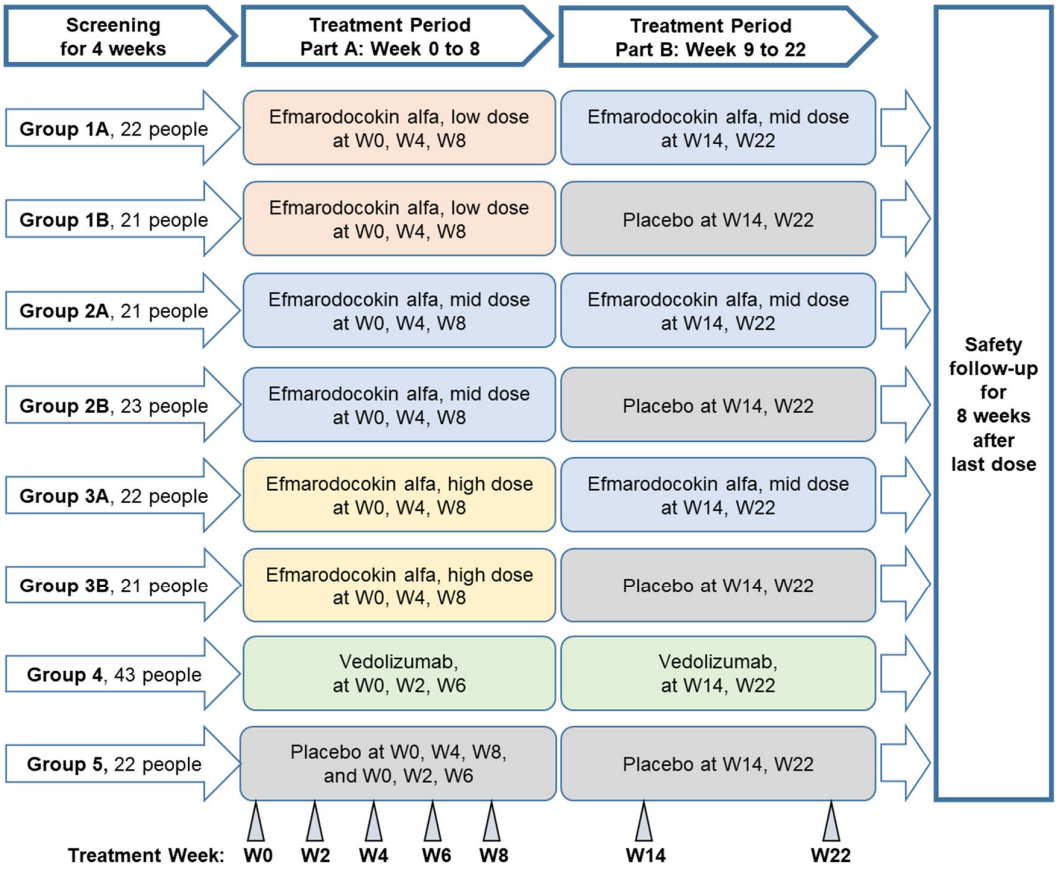
- Age between 18 and 80 years.
- They had moderate to severe UC. Doctors used imaging (endoscopy) to confirm the UC diagnosis at least 3 months before the study started.
- They had imaging (colonoscopy) within a year before the study started – that confirmed their disease met several disease criteria required for the study.
- They did not tolerate or respond to previous treatments for UC.
- People receiving ongoing treatment for UC (5-ASA, corticosteroids, probiotics) needed to be on a dose that had been stable for 2-4 weeks before study start.
- People in relationships who could get pregnant or get their partners pregnant agreed to use birth control while on the study.
- People agreed not to donate blood for 6 months after the last study treatment.

People could not take part in the study if they met any of the following conditions:

- Health conditions requiring the use of certain medicines within the previous year – corticosteroids, immunosuppressants, or biological therapy.
- Cancer within the previous 5 years.
- Poorly controlled diabetes.
- History of liver disease (sclerosing cholangitis)
- History of drug or alcohol abuse within a year of study start.
- Women who had a history of cervical abnormalities.
- Women who were pregnant, breastfeeding, or intended to get pregnant.

3. What happened during the study?

During the study, people joined a treatment group. A computer selected the treatment group at random for each person in the study. Doctors and people in the study were blinded – they did not know who was getting which treatment.



Treatments

- People who received efmarodocokin alfa got it at a low, mid, or high dose, depending on the study group they joined. These doses were 30, 60, and 90 micrograms per kilogram of body weight, written as "**µg/kg**".
- People who received vedolizumab got a standard dose – 300 µg/kg.
- Efmarodocokin alfa was given at Weeks 0, 4, 8, 14, and 22. People who were not assigned to this medicine got a placebo – so that nobody could tell who got efmarodocokin alfa.
- Vedolizumab was given at Weeks 0, 2, 6, 14, and 22. People who were not assigned to this medicine got a placebo – so that nobody could tell who got vedolizumab.
- That means everyone got two intravenous (IV) infusions at Weeks 0, 14, and 22. Everyone got one IV infusion at Weeks 2, 4, 6, and 8.
- The placebo group only got placebos – at every infusion time.

Part A: Weeks 0 to 8

- Researchers wanted to know if efmarodocokin alfa could improve people's UC symptoms.
- At Week 8, doctors performed procedures (flexible sigmoidoscopy and biopsy) – to find out if there was any response to treatments given in Part A.
- Only those patients who responded to treatments could continue to Part B.

Part B: Weeks 9 to 22

- Researchers wanted to know if improvements seen during Weeks 0-8 could last during Weeks 9 to 22. They wanted to know if this could happen with the medicine (efmarodocokin alfa or vedolizumab) or without any medicine (placebo).

Safety follow-up

- People who completed Parts A and B, and those who stopped the study – had tests done at 4 and 8 weeks after their last treatment dose.

Sponsor stopped the study

- The study stopped early because efmarodocokin alfa did not work as well as expected.

4. What were the results of the study?

Everyone in the study received at least one IV infusion and some people received up to 5. The median was 2, which means half of the people in the study received more than 2 and the other half received less than 2 IV infusions.

Treatment	People with remission at Week 8
Efmarodocokin alfa, 30 µg/kg	5 of 43 people (11.6%)
Efmarodocokin alfa, 60 µg/kg	4 of 44 people (9.1%)
Efmarodocokin alfa, 90 µg/kg	5 of 43 people (11.6%)
Vedolizumab	11 of 43 people (25.6%)
Placebo	2 of 22 people (9.1%)

Question 1: How well does efmarodocokin alfa work in comparison to vedolizumab and placebo – when given to people with UC?

Researchers looked at how many people had a "**clinical remission**". Remission is when the disease is not causing any significant symptoms or signs.

- Compared to placebo, efmarodocokin alfa did not significantly improve clinical remission at Week 8:
    - 9.1% people had remission in the placebo group.
    - 9.1% to 11.6% people had remission in the efmarodocokin alfa groups.
- Efmarodocokin alfa had a smaller remission rate (9.1% to 11.6%) in comparison to vedolizumab (25.6%).

To calculate clinical remission, researchers measured the "modified Mayo Clinical Score" or "mMCS" using three measurements – bleeding through the anus (rectal bleeding), number of bowel movements (stool frequency), and imaging (endoscopy).

Clinical remission was achieved in people whose mMCS was 2 or less, Mayo rectal bleeding subscore was 0, and other Mayo subscores were 1 or less.

This section only shows the key results from this study. You can find information about all other results on the websites at the end of this summary (see Section 8).

5. What were the side effects?

Side effects are medical problems (such as feeling dizzy) that happened during the study.

- They are described in this summary because the study doctor believed the side effects were related to the treatments in the study.
- Not all of the people in this study had all of the side effects.
- Side effects may be mild to very serious and can be different from person to person.
- It is important to be aware that the side effects reported here are from this single study. Therefore, the side effects shown here may be different from those seen in other studies, or those that appear on the medicine leaflets.
- Serious and common side effects are listed in the following sections.

Serious side effects

A side effect is considered "serious" if it is life-threatening, needs hospital care, or causes lasting problems.

During this study, one person (0.5%) had a serious side effect that the study doctors thought was caused by the study treatment. This person, who received efmarodocokin alfa 60 µg/kg, experienced low white blood cell count (**lymphopenia**).

There was one death reported in this study in a patient in Group 3A (efmarodocokin alfa 90 µg/kg) who experienced a return of UC symptoms (**UC flare**). Study doctors decided that death was not caused by the study medicine.

During the study, three people decided to stop taking their medicine because of side effects thought to be caused by the study medicine. They were in the efmarodocokin alfa treatment groups – one person each in Groups 2A, 2B, and 3A.

Most common side effects

During this study, 41 out of 195 people (21.0%) had a side effect that was not considered serious, but was thought to be caused by the study treatment.

Treatment	People with common side effects thought to be cause by the treatment
Efmarodocokin alfa, 30 µg/kg	8 of 43 people (18.6%)
Efmarodocokin alfa, 60 µg/kg	9 of 44 people (20.5%)
Efmarodocokin alfa, 90 µg/kg	13 of 43 people (30.2%)
Vedolizumab	7 of 43 people (16.3%)
Placebo	4 of 22 people (18.2%)

The most common side effects that occurred in two or more people are shown in the next table.

Number of people with side effects seen in two or more people in the study

Side effect	Efmarodocokin alfa			Vedolizumab	Placebo
	30 µg/kg	60 µg/kg	90 µg/kg		
Dry skin	3 (7%)	5 (11%)	9 (21%)	1 (2%)	1 (5%)
Feeling sick to the stomach (nausea)	0	0	2 (5%)	0	1 (5%)
Headache	0	0	0	1 (2%)	1 (5%)
Itchy skin (pruritus)	1 (2%)	0	1 (2%)	0	0
Lost sense of taste (dysgeusia)	1 (2%)	1 (2%)	0	0	0
Pimples (acne)	0	0	0	2 (5%)	0
Reddening of the skin (erythema)	(2%)	0	0	1 (2%)	0
Skin irritation or rash (dermatitis)	0	1 (2%)	0	1 (2%)	0

Other side effects

You can find information about other side effects (not shown in the sections above) on the websites listed at the end of this summary – see Section 8.

6. How has this study helped research?

The information presented here is from a single study of 195 people with UC. These results helped researchers learn more about UC and efmarodocokin alfa.

Researchers found that response to efmarodocokin alfa was not better than vedolizumab or the placebo. Researchers decided to stop this study early.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

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7. Are there plans for other studies?

At the time of writing this summary, there were no plans to study efmarodocokin alfa further.

8. Where can I find more information?

You can find more information about this study on the websites listed below:

https://clinicaltrials.gov/ct2/show/results/NCT03558152

https://www.clinicaltrialsregister.eu/ctr-search/trial/2017-002350-36/results

https://forpatients.roche.com/en/trials/autoimmune-disorder/ulcerative-colitis/a-study-to-evaluate-the-efficacy--safety--and-pharmacokinetics-o.html

Who can I contact if I have questions about this study?

If you have any further questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form – https://forpatients.roche.com/en/About.html
- Contact a representative at your local Roche office.

If you took part in this study and have any questions about the results:

- Speak with the study doctor or staff at the study hospital or clinic.

If you have questions about your own treatment:

- Speak to the doctor in charge of your treatment.

Who organized and paid for this study?

This study was organized and paid for by Genentech, Inc., South San Francisco, CA, USA. Genentech is part of F. Hoffmann-La Roche Ltd., with headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is:

Phase II, randomized, parallel-group, double-blind, double-dummy, placebo-controlled, multicenter study to evaluate the efficacy, safety, and pharmacokinetics of UTTR1147A compared with placebo and compared with vedolizumab in patients with moderate to severe ulcerative colitis.

- The study is known as “Yellowstone”.
- The protocol number for this study is GA39925.
- The ClinicalTrials.gov identifier for this study is NCT03558152.
- The EudraCT number for this study is 2017-002350-36.